Docket No. GJE-7477
Serial No. 10/517,882

Remarks

Claims 2-9 were previously pending in the subject application. By this Amendment, claims 2, 3 and 9 have been amended. No new matter has been added by these amendments. Accordingly, claims 2-9 are now before the Examiner for consideration.

The amendments to the claims have been made in an effort to lend greater clarity to the claimed subject matter and to expedite prosecution. The amendments should not be taken to indicate the applicant's agreement with, or acquiescence to, the rejections of record. Favorable consideration of the claims now presented, in view of the remarks and amendments set forth herein, is earnestly solicited.

Initially, the applicant wishes to express appreciation for the withdrawal of the previous objection to the specification, the anticipation rejection, and the obviousness rejection based on Fasmer *et al.* (1987) in view of Keller *et al.*

Claims 2-9 have been rejected under 35 U.S.C. §112, second paragraph. The Office Action indicates that the applicant's previous amendment of the claims to recite "aqueous" resulted in the introduction of new matter into the claims. However, claim 3, as originally filed, recited that the composition comprised water. Merely amending independent claims to recite a limitation that previously appeared in a dependent claim does not constitute the introduction of new matter. Therefore, the applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

Claim 9 has been rejected under 35 U.S.C. §112, second paragraph, as being indefinite. Claim 9 has been amended herein to address the issue raised by the Examiner. Accordingly, the applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. §112, second paragraph.

Claims 2-9 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Fasmer *et al.* of record in view of Williams *et al.* (WO 02/00195) of record. The applicant respectfully traverses this ground for rejection because the cited references, either alone or in combination, do not disclose or suggest the applicant's unique composition, or its intranasal use for the treatment of pain.

The subject invention provides compositions and methods whereby a specific enantiomer of nefopam is administered intranasally for the treatment of pain. While it is true that (+)-nefopam was previously known as an analgesic, nothing in the cited references suggests its particular utility for intranasal administration as claimed by the current applicant. Although the Office Action cites the Williams *et al.* reference as providing some teaching with respect to intranasal administration, it is clear from a careful reading of the Williams *et al.* disclosure that there would have been no motivation to combine Fasmer *et al.* with Williams *et al.* to arrive at the current invention.

Specifically, Williams *et al.* do not teach or even suggest that a composition comprising (+)-nefopam is suitable for application to the mucous membrane of the nasal cavity. Page 12 of the Williams et al. reference discloses nefopam (the racemate) as one of a long list of analgesics. This list is simply a laundry list of over 100 analgesics. This extensive list of analgesics is included along with similar lists of opiods, local anesthetics, mucoadhesives, preservatives, chelating agents, acids, bases, buffers, receptor antagonists, excipients, antibiotics, antifungal agents, anti-inflammatory agents, antitussive agents, expectorants, glucocorticoids, vitamins, anti-oxidants, flavoring agents, and sweetening agents (see pages 4 to 14 of the Williams *et al.* reference). Are we to believe that each and every one of these thousands of compounds (including each and every enantiomer) is particularly suited for intranasal administration? To the contrary, Williams *et al.* provide no suggestion that any of the listed compounds is particularly suitable for intranasal delivery. In this regard, please note that the Williams *et al.* reference describes administration to mucosal surfaces other than nasal mucous membranes and, in fact, the emphasis of the Williams *et al.* disclosure is on the treatment of oral mucositis. Even the Williams *et al.* passage cited in the Office Action in which Williams *et al.* refer to chemotherapy is clearly describing oral mucositis.

Therefore, even to the extent that a skilled artisan might identify a particular compound amongst the thousands of compounds listed by Williams *et al.*, it would clearly not be possible to draw any inference about the suitability of that particular compound for intranasal delivery. Accordingly, there is no reason to combine the Fasmer *et al.* reference with the Williams *et al.* reference to arrive at a composition that is particularly well suited for intranasal administration.

Then, even if Williams *et al.* and Fasmer *et al.* were combined (a combination that requires a selection of nefopam as the analgesic, (+)-nefopam as the enantiomer of interest, and assumes that administration to the nasal cavity is intended), the resultant composition would comprise, in addition to (+)-nefopam, the local anesthetic and the opioid that are essential components as described by Williams *et al.* Further, even if this unlikely selection were made, the intention of Williams *et al.* is to treat a local problem, i.e., mucosal inflammation, abrasions, ulcerations, lesions, trauma or incisions. As noted above, the emphasis of Williams *et al.* is on the treatment of local oral mucositis. It is certainly the intention of Williams *et al.* to achieve local application and effect, and to avoid systemic absorption. By contrast, the present invention achieves systemic administration of a particular analgesic that has been found to be effective. In order to achieve a systemic effect, the aim is not to treat local problems, and for that purpose a composition of the type disclosed by Williams *et al.* is unsatisfactory.

The predecessor of the Federal Circuit has opined, "[i]n determining the propriety of the Patent Office case for obviousness in the first instance, it is necessary to ascertain whether or not the reference teachings would appear to be sufficient for one of ordinary skill in the relevant art having the reference before him to make the proposed substitution, combination, or other modification." *In re Linter*, 458 F.2d 1013, 1016, 173 USPQ 560, 562 (CCPA 1972). Therefore, "[w]hen determining the patentability of a claimed invention which combines two known elements, 'the question is whether there is something in the prior art as a whole to suggest the desirability, and thus the obviousness, of making the combination.'" See *In re Beattie*, 974 F.2d 1309, 1311-12, 24 USPQ2d 1040, 1042 (Fed. Cir. 1992) (quoting *Lindemann Maschinenfabrik GmbH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1462, 221 USPQ 481, 488 (Fed. Cir. 1984)). Finally, the mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990).

It has been well established in the patent law that the mere fact that an applicant's invention contains known elements does not make the invention obvious unless there is "a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the

claimed new invention does." *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___ (2007). Furthermore, an applicant's invention is not "proved obvious merely by demonstrating that each of its elements was, independently, known in the (purported) prior art." *Id.*

An assertion of obviousness without the required suggestion or expectation of success in the prior art is tantamount to using applicant's disclosure to reconstruct the prior art to arrive at the subject invention. Hindsight reconstruction of the prior art cannot support a §103 rejection, as was specifically recognized by the CCPA in *In re Sponnoble*, 56CCPA 823, 160 USPQ 237, 243 (1969).

On page 5 of the Office Action, it is stated that "Williams *et al.* teach that nefopam comprising formulation in general are preferably applied directly to nasal cavity." The applicant has been unable to identify any such general teaching in the Williams *et al.* reference. Rather Williams *et al.* emphasize application of their composition to oral mucosal surfaces. The next sentence of the Office Action refers to the "preferred route of administration of nefopam known in the art as taught by Williams *et al.*"; clearly Williams *et al.* do not provide any such teaching.

The sentence of the Office Action bridging pages 5 and 6 states that "Williams *et al.* teach the pH suitable for intranasal application." Again, this characterization of the Williams *et al.* reference very significantly overstates the teachings of that reference with respect to intranasal administration. Williams *et al.* teach nothing particular about either (+)-nefopam or intranasal administration. In summary, Williams *et al.*, even in combination with Fasmer *et al.*, give no motivation to choose nefopam in particular, and no reason whatsoever to choose (+)-nefopam for application to the nasal cavity as claimed by the current applicant. Therefore, the applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. §103 based on Fasmer *et al.* in view of Williams *et al.*

In view of the foregoing remarks and the amendment above, the applicant believes that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

The applicant also invites the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephone interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

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